Remarks

Claims 69 through 73 are pending in this application. Claims 1 through 68 were previously cancelled by Preliminary Amendment. Claims 69 through 73 are cancelled and their subject matter is presented, in part, in a set of new claims herein. In the Response to Restriction Requirement filed January 10, 2008, Chk1 activator gemcitabine, Chk1 inhibitor Compound 281 (WO 2002/070494, page 145), and non-small cell lung cancers were elected with traverse. The pending claims stand rejected under 35 U.S.C. §103. This paper contains amendments under 37 C.F.R. §1.121. Support for the amendments to the claims can be found in the specification, for example, at page 151, line 28 through page 152, line 2 and in WO 2002/070494 – which is incorporated by reference as provided, at minimum, on page 13, line 21 through page 25, line 9 in the present application – at page 22, line 27 through page 27, line 33; pages 201, 216, and 217, which correspond to original Claims 6, 22, and 24; pages 137 through 138, which corresponds to Compound 260; and page 145, which corresponds to Compound 281.

Election/Restrictions

Applicants respectfully note the Office's comments regarding election and restriction as provided.

Rejection of Claims 69 through 73 under 35 U.S.C. §103(a)

Claims 69 through 73 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Keegan et al. (WO 2002/070494) in view of Gandhi et al. Applicants respectfully disagree with this rejection.

In order to be completely responsive to this Office Action, Applicants respectfully note that the subject matter of the various claims were commonly owned at the time the inventions were made.

The factual inquiries set forth in *Graham v. John Deere Co.,* 383 U.S. 1 (1966) are employed when making an obviousness analysis. Those factual inquiries include: 1) determining the scope and contents of the prior art; 2) ascertaining the differences between the prior art and the claims in issue; 3) resolving the level of ordinary skill in the pertinent art; and 4) evaluating evidence of secondary considerations. A finding of obviousness under 35 U.S.C. §103(a) requires that the prior art suggest the claimed invention, as a whole, to one of ordinary skill in the art. Thus, the obviousness inquiry of 35 U.S.C. §103(a) requires a factual comparison of the claimed subject matter to the relevant art. To render a claim obvious, the prior art must be such as to lead

one of ordinary skill in the art to arrive at the claimed invention with a reasonable expectation of success. (See MPEP 2141 I. and II.)

The Office focuses upon gemcitabine, Compound 281 (WO 2002/070494, page 145), and non small cell lung cancer as "the elected species of Chk1 activator, Chk1 selective inhibitor and cell proliferative disorder currently under examination." The Office points to the teachings in Keegan et al. regarding administration of gemcitabine and Compound 281 as well as non small cell lung cancer. The Office then notes that Keegan et al. does not teach administration of gemcitabine for from about 30 minutes to about 96 hours or from about 30 minutes to [about] 48 hours. The Office then indicates that Gandhi et al. teaches administration of gemcitabine for twelve hours without untoward toxicity and that this prolonged infusion derives the maximum cytotoxic advantage. The Office also notes that Keegan et al. does not teach administration of Compound 281 for from up to about 1 for from up to about 72 hours following the administration of gemcitabine but "does teach that gemcitabine and [C]ompound 281 can be administered in multiple doses at different intervals." Furthermore, the Office indicates that Keegan et al. "does not explicitly teach that the administration of gemcitabine synchronizes cell cycle arrest among the tumor cells; however this is a property of the composition and is necessary present." As noted above, Applicants respectfully disagree with this rejection.

As noted by the Office, Keegan et al. does contain teachings regarding gemcitabine, Compound 281, and treatment of cancer, including lung carcinomas, but does not teach the administration of gemcitabine for from about 30 minutes to about 96 hours or from about 30 minutes to [about] 48 hours nor the administration of Compound 281 for from up to about 1 for from up to about 72 hours following the administration of gemcitabine (emphasis added). The Office also looks to page 50, lines 20 and 21 in Keegan et al. as indicating that "gemcitabine and [c]ompound 281 can be administered in multiple doses at different intervals" and would have been obvious to the skilled artisan "to optimize the sequence of administration and infusion duration to determine the regimen with maximum efficacy...." First of all, the noted disclosure in Keegan et al. states that "[t]he desired dose can be conveniently administered in a single dose, or as multiple doses administered at appropriate intervals, for example as two, three, four or more subdoses per day." Applicants respectfully indicate that this disclosure is directed to administration of a selective Chk1 inhibitor alone and does not have anything to do with administration of a Chk1 activator. Furthermore, Applicants assert that the present invention provides that pretreatment with a Chk1 activator prior to administration of a selective Chk1 inhibitor leads to greater anti-tumor activity than co-administration of the two agents together and

reduces the required exposure time to a Chk1 inhibitor to result in tumor cell death (see Examples 1 and 2, page 159, line 9 through page 161, line 20, of the present application). Additionally, the Office indicates and Applicants agree that Keegan et al. does not explicitly teach that administration of gemcitabine synchronizes cell cycle arrest among the tumor cells. Indeed, Chk1 activator cell cycle arrest synchronization is not the sole facet of the present claims. Instead, it is the combination of the contact of at least one Chk1 activator for a time within a particular range in an amount sufficient to substantially synchronize cell cycle arrest followed by contact with a selective Chk1 inhibitor for a time within a particular range in an amount sufficient to substantially abrogate said cell cycle arrest that substantiate the subject matter of the present claims. Thus, in view of all of the aforementioned points, Keegan et al. does not direct the skilled artisan toward the particular dosing regimen in the present claims and, therefore, does not render the present claims obvious.

Turning to Gandhi et al., the Office points out that this reference teaches administration of gemcitabine for twelve hours without untoward toxicity and that this prolonged infusion derives the maximum cytotoxic advantage. While Applicants note that Gandhi et al. provided patients with gemcitabine for up to 18 hours, that reference has no teaching whatsoever about subsequent administration of a selective Chk1 inhibitor. As such, Gandhi does not direct the skilled artisan, either alone or in combination with the teachings in Keegan et al., to the present claims directed to a particular dosing regimen. As such, the present claims are not obvious in view of Gandhi et al.

In view of the aforementioned aspects of the cited references, Applicants respectfully assert that the present claims differ from the teachings supplied by these cited references. As clearly evidenced by these references, there is no teaching or suggestion whatsoever that would yield the present claims. Also, the cited references provide no motivation to make the changes necessary to arrive at the present claims. Thus, Applicants respectfully request withdrawal of this rejection.

Conclusion

Applicants assert that the above-stated remarks overcome the Office's rejection for this application. Applicants courteously solicit reconsideration of this rejection and passage of this case to issuance.

Respectfully submitted,

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